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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,405	07/24/2002	Baskaran Chandrasekar	410718.90395	2963

7590 09/09/2005

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EXAMINER	
COTTON, ABIGAIL MANDA	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 09/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,405	CHANDRASEKAR ET AL.	
	Examiner	Art Unit	
	Abigail M. Cotton	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 3/18/02,7/19/02,7/24/02,8/2/02,7/9/03. 5/18/04 and 5/5/05

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-8 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-8 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3/18/02,7/19/02 and 5/18/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-8 are pending in the application as of the amendment received on August 2, 2002.

Priority

Applicant's claim of foreign priority to CA 2,282,982 and CA 2,300,246 is acknowledged.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-8 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, because while the claims provide for the "use" of 17-beta estradiol, the claims do not set forth any steps involved in the method/process, and thus it is unclear what method/process applicant they are intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. See for example *Ex parte Erlich,* 3 USPQ2d 1011 (Bd. Pat. App. & Inter. 1986.) Appropriate correction is required.

Claims 1-8 are furthermore rejected under 35 U.S.C. 112, second paragraph, as being indefinite because it is not clear whether the claims are directed to a method of administering a medication having 17-beta estradiol in the lumen of a blood vessel having suffered vascular injury, or whether the claim is directed to a method of making a medication having 17-beta estradiol, in which administration in the lumen of a blood vessel is merely the intended use of said medication. Accordingly, as the scope of the claim cannot be determined, the claim is indefinite under 35 U.S.C. 112, second paragraph. Appropriate correction and/or clarification is required.

In the interests of compact prosecution and for the purposes of applying prior art, the claims are being interpreted as being directed to a method of administering the claimed medication comprising 17-beta estradiol.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for lacking antecedent basis for the term "said pharmaceutically acceptable carrier," as recited in the claim. Claim 1, from which claim 5 depends, recites a "medication" but does not recite a "pharmaceutically acceptable carrier." Accordingly, claim 5 is indefinite under 35 U.S.C. 112, second paragraph, because it is not clear what pharmaceutically acceptable carrier is intended. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,866,561 to Mark T. Ungs, issued February 2, 1999.

Ungs teaches a method for inducing angiogenesis in blood vessels proximal to stenosed regions, including application of an estrogen compound to the blood vessel walls at a treatment site proximal to or upstream of the stenosis (see abstract, in particular.) Ungs teaches that restenosis following PTCA is a signification problem, and that administration of estrogen to the stenosed, dilated region after PTCA has been suggested for the purposes of preventing restenosis (see column 1, lines 10-20 and 40-52, in particular.) Ungs teaches that it is thus desirable to increase perfusion to heart tissue in place of or in addition to PTCA treatment (see column 1, lines 54-65, in particular.) Ungs teaches that a preferred method of treating stenosis involves application with a double walled drug delivery balloon catheter, as well as by coating a stent with an estrogen compound or by puncturing a vessel wall (see column 2, lines 5-45, in particular.) Ungs teaches that preferred estrogen compounds include 17-Beta estradiol (see column 4, lines 1-12, in particular.) Accordingly, Ungs teaches administration of 17-Beta estradiol in the lumen of a blood vessel having suffered vascular injury. Ungs furthermore teaches single administration of 17-Beta estradiol, as Ungs teaches the compound can be administered via a stent or balloon catheter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,866,561 to Mark T. Ungs, issued February 2, 1999, as applied to claims 1 and 8 above, and further in view of U.S. Patent No. 5,512,557 to Peter Collins, issued April 30, 1996.

Ungs is applied as discussed above, and teaches administration of 17-Beta estradiol in the lumen of a blood vessel having suffered vascular injury. Ungs does not specifically teach administration in the unit doses recited in claims 2-4.

Collins teaches that 17-beta estradiol can be provided to teat coronary heart disease (see abstract, in particular.) Collins teaches that a suitable dose may be delivered in various forms, depending upon the route of administration, such as oral or parenteral administration (see column 2, lines 1-15, in particular) and the dosage may be varied according to the symptoms, age and body weight of the patient (see column 2, lines 15-25, in particular.) Collins teaches that a suitable daily dose may be from 0.5 mg to 2 mg (see column 2, lines 15-25.) Assuming administration of the dose to a female patient having a weight of about 65 Kg (~130 lbs), the dose is equivalent to a daily dose of about 8 micrograms/kg to about 30 micrograms/Kg, which meets and/or closely overlaps with the does ranges recited in the claims. Furthermore, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to optimize dose unit according to patient weight, means of

administration, etc, in light of the teachings of Collins, to provide a desired dosage of the 17-B estradiol. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

Accordingly, one of ordinary skill in the art at the time the invention was made would have found it obvious to provide the dosage taught by Collins in the vascular injury treatment and estrogen delivery method of Ungs, because Collins teaches that the dose is capable of showing beneficial cardiovascular effects. Thus, one of ordinary skill in the art would have been motivated to deliver 17-beta estradiol by the method of Ungs and in the dosage of Collins, with the expectation of providing an effective dosage capable of yielding cardiovascular treatment.

Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,866,561 to Mark T. Ungs, issued February 2, 1999, as applied to claims 1 and 8 above, and further in view of U.S. Patent No. 4,727,064 to Josef Pitha, issued February 23, 1998.

Ungs is applied as discussed above, and teaches administration of 17-Beta estradiol in the lumen of a blood vessel having suffered vascular injury, for example via catheter. Ungs does not specifically teach administration of hydroxypropyl-beta-cyclodextrin (HPCD) as recited in claims 5-7.

Pitha teaches that pharmaceutical preparations containing cyclodextrin derivatives have enhanced dissolution properties and thus enhanced absorption by the body (see abstract, in particular.) Pitha teaches that cyclodextrin mixtures effectively solubilize liphophilic drugs in aqueous media, and have low toxicity (see column 2, lines 35-60, in particular.) Pitha demonstrates that estradiol is a drug that exhibits improved solubility in combination with hydroxypropyl-beta-cyclodextrin (see Table I, in particular.) Accordingly, Pitha teaches the benefits in improved solubility and absorption of providing estradiol in combination with hydroxypropyl-beta-cyclodextrin.

Regarding the dosage amount recited in claim 7, Pitha teaches that the cyclodextrin additives may generally be utilized in a weight percent of from about 40-60% of the drug solution (see column 2, lines 62-68, in particular.) Pitha furthermore teaches intraperitoneal injection of hydroxypropyl-beta-cyclodextrin into mice was non-fatal at 3.2g/kg, and teaches a lack of oral toxicity of the hydroxypropyl-beta-cyclodextrin (see column 4, line 64 through column 5, line 5, in particular.) Accordingly, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to optimize the amount of hydroxypropyl-beta-cyclodextrin provided in the medication, according to the guidelines provided by Pitha, to provide the desired solubility and absorption characteristics of the estradiol. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not

inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

Accordingly, one of ordinary skill in the art at the time the invention was made would have found it obvious to provide the hydroxypropyl-beta-cyclodextrin of Pitha in the 17-beta estradiol delivery method of Ungs, with the expectation of improving the solubility and absorption of the 17-beta estradiol compound in the patient.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abigail M. Cotton whose telephone number is (571) 272-8779. The examiner can normally be reached on 8:30-5:00, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AMC

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER